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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,663	08/01/2003	Alena Donda	NY-LUD 5673.1-US	3562

24972 7590 02/22/2007
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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,663	DONDA ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 11/17/06 is acknowledged and has been entered.

2. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). Misnumbered claims 16-21 been renumbered 22-30.

3. Applicant is reminded of Applicant's election of the species of A is a Fab' fragment specific for CEA, B is bis maleimide polyethylene oxide, and C is one HLA-A2 molecule complexed with SEQ ID NO: 1 (influenza peptide GILGFVFTL) in Applicant's amendment and response filed 3/9/06.

Claims 22-30 are presently being examined.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The oath or declaration is defective because: the filing date of the 10/276,764 parent application is listed as 11/19/02, whereas the filing date is 2/10/03.

5. The replacement drawings filed 11/17/06 are objected to because the Y-Axis values for Figures 2B and 3B as well as some of the Y-Axis numerical values are handwritten. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the Examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

6. If Applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, 121 or 365(c), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (*i.e.,* continuation, divisional, or continuation-in-part) of the applications.

It is noted by the Examiner that in Applicant's amendment filed 11/17/06, the first line of the specification references Serial No. 10/276,764 and now lists the correct filing date of 2/10/03. However, the relationship of the '764 application must be correctly disclosed. The said amendment discloses "The application is a ***continuation in fact*** *of application Serial No. 10/276,76", rather than 'This application is a continuation in part.'*

The following are new grounds of rejection necessitated by Applicant's amendment filed 11/17/06.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 22-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the specification and claims as originally filed is as follows: A fusion protein of the formula recited in instant claim 22, wherein the protein or polypeptide is linked via bis-maleimide polyethylene oxide to the MHC/peptide complex, *i.e.,* wherein the two polypeptide portions of a "fusion protein" are linked via an inorganic chemical compound that is bis-maleimide polyethylene oxide (*i.e.,* the claimed product is really a conjugate, not a fusion protein).

9. Claims 22-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a conjugate comprising the formula recited in instant claim 22, and including those recited in the dependent claims, does not reasonably provide enablement for a "fusion protein" of the recited formula. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification does not disclose how to make the instant invention, a fusion protein of the formula recited in instant claim 22 and including those recited in the dependent claims 23-30. The specification has not enabled the breadth of the claimed invention because the claims encompass a fusion protein wherein the first polypeptide or peptide portion that binds specifically to a target cell surface and the second protein, the MHC/peptide complex, is bound via an inorganic chemical compound that is bis-maleimide polyethylene oxide rather than by a peptide bond.

The specification discloses production of conjugates of monomeric MHC peptide complexes with a single murine Fab' specific for CEA by chemical conjugation of the MHC/peptide complexes with an excess of bis-maleimide polyethylene oxide, removal of excess coupling reagent by gel filtration and reaction of the resulting bis-maleimide derivatized MHC complexes containing a free thiol group at position 275 with an excess of reduced Fab' fragments, and purification of the resulting conjugates via FPLC (especially Example 2). The specification further discloses: "[0127] When "B" is not present in the complexes, "A" and "C" may be prepared via the use of e.g., nucleic acid coding constructs which encode fusion polypeptides. Such techniques are well known, as is described, supra. One may also modify the elements "A" and "C" to connect them chemically, as was shown in the examples. One may add amino acid sequences such as those found in the Jun and Fos oncogenes, which then bind A and C via leucine zipper formation. Other alternatives are available, which the skilled artisan will note. [0128] When "B" is used, this comprises a molecule or molecules which facilitates the linking of "A" and "C." B can also comprise a specific binding pair of molecules, or a complex thereof, such as a complex of avidin or streptavidin or a chemically modified form of streptavidin or avidin, and anywhere from 1 to 4 biotin molecules. For example, B can be a bispecific antibody with one arm directed against a "Tag" epitope placed at the C terminus of A, and the other arm directed against another "Tag" epitope placed at the C terminus of C. The number of binding antibody fragments may vary. Preferably, from 1-5 are used. One may also use, e.g., a bifunctional antibody, or any other molecule or molecular complex to which "A" and "C" can both be joined such as an additional antibody, or binding fragment of an antibody. In particular, an additional antibody fragment which has the property of activating the T lymphocytes, such as anti-CD-28 antibody or a recombinant ligand, such as B7.1, B7.2, or IL-2 for a receptor that activates T lymphocytes, may be used. These additional materials may be linked to a free cysteine, residue on the first Fab' fragment from the Fab-MHC conjugate. The use of free cysteine on a bispecific antibody to synthesize trispecific antibodies is taught by

Tutt, et al., J. Immunol., 147:60-69 (1991), incorporated by reference. If fusion proteins are used, then a single cysteine residue allowing the coupling of the T lymphocyte activating, third molecule, can be introduced via, e.g., site specific mutation between the two partners of the fusion protein."

Evidentiary reference Biology-Online.org teaches that a fusion protein is a protein formed by expression of a hybrid gene made by combining two gene sequences, and typically this is accomplished by cloning a cDNA into an expression vector in frame with an existing gene.

Evidentiary reference Cancer.govPatient teaches that a fusion protein is a protein created by joining two genes together, and that fusion proteins may occur naturally or can be created in the laboratory.

There is insufficient guidance in the specification as to how to make the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 22-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite in the recitation of "fusion protein of formula: ...wherein B is bis-maleimide polyethylene oxide..." because it is not clear what is meant, *i.e.,* how a fusion protein can have a chemical linkage of two portions using the chemical linker is bis-maleimide polyethylene oxide.

12. Applicant's claim amendments have overcome the prior art rejections of record and the double patenting rejection of record.

13. Claims 22-30 are free of the prior art.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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